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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/588,902

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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/588,902	<b>Applicant(s)</b> GILLESPIE ET AL.	
	<b>Examiner</b> /Venkataraman Balasubramanian/	<b>Art Unit</b> 1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 23-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 23 and 26 is/are allowed.
- 6) ☒ Claim(s) 24 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicants' response, which included cancellation of claims 1-22, 27-42 and amendment to claim 23, filed on 09/03/2010, is made of record. Claims 23-26 are now pending. In view of applicants' response, the 112 second paragraph rejection, 112 first paragraph rejections and provisional double patenting rejections have been obviated. However, the following new grounds of rejections are applied to currently pending claims.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 24 is indefinite as it recites a Table I but there is no such Table I in claim 24. It is not clear what compounds are referred to and whether they are within the scope of claim 23. An appropriate correction is needed.
2. Claim 25 is indefinite as it does not recite to whom the compound is administered and who is in need of such therapy. An appropriate correction is needed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating hypertension does not reasonably provide enablement for therapy of any or all disorders or diseases in a subject as generically embraced in claim 25. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with the claim.

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." See MPEP 2164.01(a). The factors to be considered in making an enablement rejection have been summarized below.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention:

Therapeutic use of the compounds in treating pathological disorders/diseases that require purine receptor blocking activity. The instant method of use claim 25 is drawn to a therapy by administering an effective amount of compound of formula I of claim 23 and thereby reds any therapy of any or all diseases and disorders for which there is no enabling disclosure.

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Instant claims as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the blocking of purine receptor in general and adenosine receptor in general by the instant compounds, the method of use claims reach through treating any or all disorders and diseases mediated purine receptor and more specifically adenosine receptor indicated above and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of adenosine receptor or purine receptor, based on limited in vitro assay with limited enzyme, it is claimed that treating any or all disorders and diseases including movement disorders; anxiety disorders, affective disorders; central and peripheral nervous system degenerative disorders; schizophrenia; cognitive and memory impairment disorders; attention disorders; central nervous system injury; cerebral ischaemia; myocardial ischaemia; muscle ischaemia; sleep disorders; eye disorders; cardiovascular disorders; and diabetes, Parkinson's disease, progressive supranuclear palsy, Huntingtons disease, multiple system atrophy, corticobasal degeneration, Wilsons disease, Hallerorden-Spatz disease, progressive pallidal atrophy, Dopa-responsive dystonia-Parkinsonism and spasticity, the anxiety disorders selected from panic disorder, agoraphobia, obsessive compulsive disorder, social phobia, post traumatic stress disorder, generalized anxiety disorder and specific phobia, affective

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disorders selected from bipolar disorder, seasonal affective disorder, depression, manic depression, atypical depression and mono depressive disease, central and peripheral nervous system degenerative disorders selected from corticobasal degeneration, demyelinating disease, Freidrich's ataxia, motoneurone disease, multiple system atrophy, myelopathy, radiculopathy, peripheral neuropathy, systemic lupus erythamatosi, granulomatous disease, olivo-ponto-cerebellar atrophy, progressive pallidal atrophy, progressive supranuclear palsy and spasticity, cognitive and/or memory, impairment disorders selected from dementia, Alzheimers Disease, Frontotemporal dementia, multi-infarct dementia, AIDS dementia, dementia associated with Huntingtons Disease, Lewy body dementia, senile dementia, age-related memory impairment, cognitive impairment associated with dementia, Korsakoff syndrome, dementia pugilans, attention disorders selected from attention-deficit hyperactivity disorder (ADHD), attention deficit disorder, minimal brain dysfunction, brain-injured child syndrome, hyperkinetic reaction childhood and hyperactive child syndrome, central nervous system injuries selected from traumatic brain injury, surgical trauma, raised intracranial pressure, cerebral oedema, hydrocephalus and spinal cord injury, cerebral ischaemia such as transient ischaemic attack, stroke, subarachnoid haemorrhage, cerebral vasospasm, perinatal asphyxia, drowning, cardiac arrest or subdural haematoma, sleep disorders selected from hypersomnia, narcolepsy and restless legs syndrome, eye disorders selected from retinal ischaemia-reperfusion injury and diabetic neuropathy, and neuroprotection for all of which there is no enabling disclosure.

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In addition, the scope of the claim is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 1-3 and 27-29. The instant compounds are disclosed to have purine and adenosine receptor inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action adenosine receptor inhibitor that would be useful for all sorts of generic diseases and disorders, including those listed above. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host.

The scope of the claims involves all of the millions of compounds of claim 23 as well as the thousands and thousands of diseases embraced in claim 25.

Similarly, enablement for the scope of "any disorder" generally is not present. For a compound or genus to be effective against any disorder based on mode of action generally is contrary to medical science. The claims cover methods for treatment of all of the diseases mentioned above, including other diseases that may be discovered in the future that may be comprehended under the recited diseases.

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the

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uses disclosed and embraced by the claim language for the intended mammal. Moreover many if not most of diseases cited above are very difficult to treat and hardly possible to prevent as claimed herein.

No compound has ever been found to treat any or all diseases and disorders of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “compound” is contrary to our present understanding of modern medicine. The specification fails to identify the results of treatment with the methods of this invention and how such results would be recognized, particularly with regard to conditions and diseases that are currently considered incurable, untreatable or fatal.

Note substantiation of utility and its scope is required when utility is “speculative”, “sufficiently unusual” or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that ‘a claimed invention must have a specific and substantial utility’. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See *Sitkovsky*, *Baraldi* and *Gao* provided.



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Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

2) The state of the prior art: Recent publications expressed that the adenosine receptor inhibition effects are unpredictable and are still exploratory. See Sitkovsky et al., British Journal of Pharmacology, 153, 5457-5464, 2008, especially the concluding paragraph. See also Baraldi et al., European Journal of Medicinal Chemistry 38: 367-382, 2003. See also Gao et al., Expert. Opin. Emerging Drugs 12(3): 479-492, 2008, which indicates the state of the art and points out need for further experimentation to establish the usefulness of antagonists of adenosine receptors.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all disorders stated above with the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all

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condition and diseases stated above and the state of the art is that the effects of adenosine receptor inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace any or all disorders, and including those yet to be related to purine or adenosine receptor activity with a large genus of compounds.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

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engage in undue experimentation to test which diseases can be treated by the compounds encompassed in the instant claims, with no assurance of success.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection same as that made in the previous office action but now applied to only claim 25, inclusion of which in the previous office action was inadvertently omitted.

#### ***Allowable Subject Matter***

Claims 23 and 26 are allowed.

#### **Conclusion**

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624